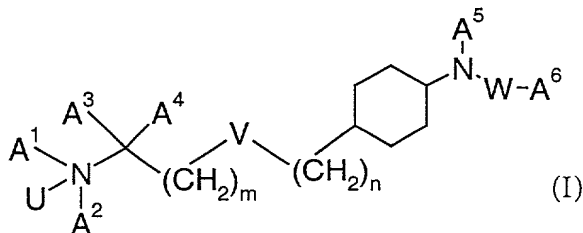


Claims

1. A compound selected from the group consisting of compounds of formula (I)



wherein

U is O or a lone pair;

V is O, S, -CH₂-, -CH=CH-, or -C≡C-;

W is CO, COO, CONR¹, CSO, CSNR¹, SO₂, or SO₂NR¹;

m and n are each integers from 0 to 7, with the provisos that m+n is 0 to 7 and m is not 0 when V is O or S;

A¹ is H, lower-alkyl, hydroxy-lower-alkyl, or lower-alkenyl and

A² is lower-alkyl, cycloalkyl, cycloalkyl-lower-alkyl, or lower-alkenyl, optionally substituted by R², or

A¹ and A² bond together to form -A¹-A²-, wherein -A¹-A²- is lower-alkylene or lower-alkenylene, optionally substituted by R², in which one -CH₂- group of -A¹-A²- is optionally replaced by NR³, S, or O;

A³ and A⁴ are each hydrogen or lower-alkyl, or

A³ and A⁴ bond together to form -A³-A⁴-, wherein -A³-A⁴- is -(CH₂)₂₋₅- optionally mono- or multiply-substituted by lower-alkyl;

A⁵ is H, lower-alkyl, lower-alkenyl, or aryl-lower-alkyl;

A⁶ is lower-alkyl, cycloalkyl, aryl, aryl-lower-alkyl, heteroaryl, heteroaryl-lower-alkyl, lower-alkoxy-carbonyl-lower-alkyl;

R² is hydroxy, hydroxy-lower-alkyl, lower-alkoxy, lower-alkoxycarbonyl, N(R⁴,R⁵), or thio-lower-alkoxy;

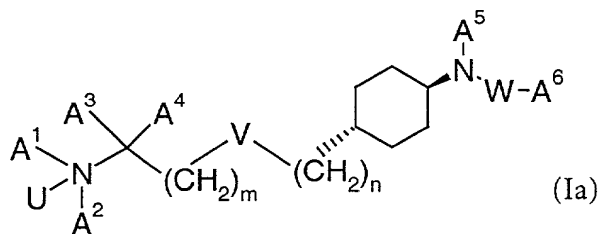
R¹, R³, R⁴ and R⁵ independently from each other are hydrogen or lower-alkyl; and

when A¹ is not bonded to A² and A³ is not bonded to A⁴, A¹ and A³ optionally bond together to form -A¹-A³-, wherein -A¹-A³- is lower-alkylene or lower-alkenylene, optionally substituted by R², in which one -CH₂- group of -A¹-A³- is optionally replaced by NR³, S, or O;

pharmaceutically acceptable salts of the compounds of formula (I), and

pharmaceutically acceptable esters of the compounds of formula(I).

2. The compound according to claim 1, wherein A³ and A⁴ are not bonded together.
3. The compound according to claim 1, selected from the group consisting of compounds of formula (Ia)



wherein U, V, W, m, n, A¹, A², A³, A⁴, A⁵ and A⁶ are as defined in claim 1;

pharmaceutically acceptable salts of the compounds of formula (Ia); and

pharmaceutically acceptable esters of the compounds of formula (Ia).

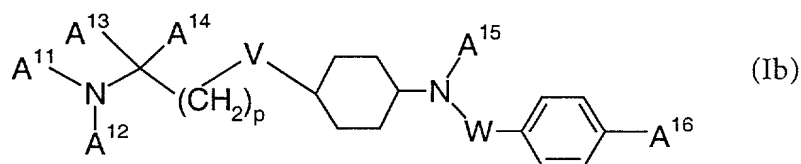
4. The compound according to claim 1, wherein U is a lone pair.
5. The compound according to claim 4, wherein V is O.
6. The compound according to claim 4, wherein V is -CH₂-.
7. The compound according to claim 4, wherein V is -C=C-.
8. The compound according to claim 4, wherein V is -C≡C-.
9. The compound according to claim 4, wherein W is CO, COO, CONR¹, CSNR¹, SO₂ or SO₂NR¹ and R¹ is hydrogen.
10. The compound according to claim 9, wherein W is COO or SO₂.

11. The compound according to claim 10, wherein n is 0.
12. The compound according to claim 10, wherein n is 1.
13. The compound according to claim 10, wherein m is 1 to 6.
14. The compound according to claims 10, wherein m is 0 and V is $-C=C-$ or $-C\equiv C-$.
15. The compound according to claim 10, wherein A^1 is H, methyl, ethyl, isopropyl, 2-hydroxy-ethyl, or 2-propenyl.
16. The compound according to claim 10, wherein A^2 is lower-alkyl, cycloalkyl-lower-alkyl, or lower-alkenyl, optionally substituted with R^2 , wherein R^2 is hydroxy, methoxy, or ethoxycarbonyl.
17. The compound according to claim 16, wherein A^2 is methyl, ethyl, 2-hydroxy-ethyl, 2-propenyl, propyl or isopropyl.
18. The compound according to claim 10, wherein A^1 and A^2 are bonded together.
19. The compound according to claim 18, wherein $-A^1-A^2-$ is lower-alkylene or lower-alkenylene, optionally substituted by R^2 , in which one $-CH_2-$ group of $-A^1-A^2-$ can optionally be replaced by O, wherein R^2 is hydroxy or 2-hydroxyethyl.
20. The compound according to claim 19, wherein $-A^1-A^2-$ is $-(CH_2)_5-$.
21. The compound according to claim 10, wherein A^3 is hydrogen.
22. The compound according to claim 10, wherein A^4 is hydrogen.
23. The compound according to claim 10, wherein A^3 and A^4 are bonded together to form $-A^3-A^4-$, and $-A^3-A^4-$ is $-(CH_2)_2-$.

24. The compound according to claim 10, wherein A⁵ is H, lower-alkyl, lower-alkenyl, or benzyl optionally substituted with halogen.
25. The compounds according to claim 24, wherein A⁵ is methyl or ethyl.
26. The compound according to claim 25, wherein A⁶ is lower-alkyl, cycloalkyl, phenyl, naphthyl, phenyl-lower-alkyl, pyridyl, indolyl, indolynyl, thienyl, thienyl-methylene, furyl-methylene, benzodioxyl, chinolyl, isoxazolyl, or imidazolyl, optionally substituted by one or more substituents selected from the group consisting of lower-alkyl, lower-alkoxy, lower-alkylcarbonyl, lower-alkoxycarbonyl, fluorine, chlorine, bromine, CN, CF₃, NO₂, or N(R⁶,R⁷), wherein R⁶ and R⁷ independently from each other are hydrogen or lower-alkyl.
27. The compound according to claim 26, wherein A⁶ is phenyl optionally substituted by one or more substituents selected from the group consisting of fluorine, chlorine, bromine, and CF₃.
28. The compound according to claim 27, wherein A⁶ is 4-chloro-phenyl, 4-bromo-phenyl, or 4-trifluoromethyl-phenyl.
29. The compound according to claim 28, wherein A¹ is H, lower alkyl or hydroxy-lower alkyl and A² is lower alkyl, hydroxy-lower alkyl or lower alkenyl.
30. The compound according to claim 29, wherein A³ and A⁴ are hydrogen.
31. The compound according to claim 30, wherein V is O.
32. The compound according to claim 30, wherein V is S.
33. The compound according to claim 32, selected from the group consisting of trans-{4-[2-(Allyl-methyl-amino)-ethylsulfanylmethyl]-cyclohexyl}-methyl-carbamic acid 4-

chloro-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

34. The compound according to claim 30, wherein V is -CH₂-.
35. The compound according to claim 30, wherein V is -C=C-.
36. The compound according to claim 30, wherein V is -C≡C-.
37. A compound selected from the group consisting of compounds of formula (Ib)



wherein

V is O, S, -CH₂-, -CH=CH-, or -C≡C-;

W is COO or SO₂;

p is an integer from 0 to 7, with the proviso that p is not 0 when V is O or S;

A¹¹ is H, lower-alkyl, or hydroxy-lower-alkyl and

A¹² is lower-alkyl, hydroxy-lower alkyl, or lower-alkenyl, or

A¹¹ and A¹² bond together to form -A¹-A²-, wherein -A¹-A²- is lower-alkylene;

A¹³ and A¹⁴ are each hydrogen or bond together to form -A³-A⁴-, wherein -A³-A⁴- is -
(CH₂)₂₋₅-;

A¹⁵ is lower-alkyl; and

A¹⁶ is halogen or trifluoromethyl;

pharmaceutically acceptable salts of the compounds of formula (Ib), and

pharmaceutically acceptable esters of the compounds of formula(Ib).

38. The compound according to claim 37, wherein A¹¹ is H, lower-alkyl, or hydroxy-lower-alkyl and A¹² is lower-alkyl, hydroxy-lower alkyl, or lower-alkenyl.

39. The compound according to claim 38, selected from the group consisting of trans-N-{4-[2-(1-dimethylamino-cyclopropyl)-ethoxy]-cyclohexyl}-N-methyl-4-trifluoromethyl-benzenesulfonamide, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.
40. The compound according to claim 37, whereon A¹³ and A¹⁴ are hydrogen.
41. The compound according to claim 40, selected from the group consisting of trans-4-bromo-N-methyl-N-[4-(2-piperidin-1-yl-ethoxy)-cyclohexyl]-benzenesulfonamide, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.
42. The compound according to claim 40, selected from the group consisting of trans-methyl-[4-(4-piperidin-1-yl-butyl)-cyclohexyl]-carbamic acid 4-bromo-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.
43. The compound according to claim 40, selected from the group consisting of trans-N-methyl-N-[4-(4-piperidin-1-yl-butyl)-cyclohexyl]-4-trifluoromethyl-benzenesulfonamide, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.
44. The compound according to claim 40, selected from the group consisting of trans-methyl-[4-(5-piperidin-1-yl-pentyl)-cyclohexyl]-carbamic acid 4-chloro-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.
45. The compound according to claim 40, wherein A¹¹ is H, lower-alkyl, or hydroxy-lower-alkyl and A¹² is lower-alkyl, hydroxy-lower alkyl, or lower-alkenyl.
46. The compound according to claim 45, wherein V is O.

47. The compound according to claim 46, wherein W is COO.
48. The compound according to claim 47, selected from the group consisting of trans-{4-[6-(allyl-methyl-amino)-hexyloxy]-cyclohexyl}-methyl-carbamic acid 4-chloro-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.
49. The compound according to claim 47, selected from the group consisting of trans-{4-[4-(allyl-methyl-amino)-butoxy]-cyclohexyl}-methyl-carbamic acid 4-trifluoromethyl-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.
50. The compound according to claim 47, selected from the group consisting of trans-(4-{4-[ethyl-(2-hydroxy-ethyl)-amino]-butoxy}-cyclohexyl)-methyl-carbamic acid 4-trifluoromethyl-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.
51. The compound according to claim 47, selected from the group consisting of trans-[4-(4-dimethylamino-butoxy)-cyclohexyl]-methyl-carbamic acid 4-trifluoromethyl-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.
52. The compound according to claim 47, selected from the group consisting of trans-{4-[4-(allyl-methyl-amino)-butoxy]-cyclohexyl}-methyl-carbamic acid 4-chloro-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.
53. The compound according to claim 46, wherein W is SO₂.
54. The compound according to claim 53, selected from the group consisting of trans-N-[4-(3-allylamino-propoxy)-cyclohexyl]-N-methyl-4-trifluoromethyl-

benzenesulfonamide, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

55. The compound according to claim 53, selected from the group consisting of trans-N-[4-(6-diethylamino-hexyloxy)-cyclohexyl]-N-methyl-4-trifluoromethyl-benzenesulfonamide, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.
56. The compound according to claim 53, selected from the group consisting of trans-N-[4-(4-dimethylamino-butoxy)-cyclohexyl]-N-ethyl-4-trifluoromethyl-benzenesulfonamide, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.
57. The compound according to claim 53, selected from the group consisting of trans-N-ethyl-N-(4-{4-[(2-hydroxy-ethyl)-methyl-amino]-butoxy}-cyclohexyl)-4-trifluoromethyl-benzenesulfonamide, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.
58. The compound according to claim 53, selected from the group consisting of trans-N-(4-{4-[bis-(2-hydroxy-ethyl)-amino]-butoxy}-cyclohexyl)-N-ethyl-4-trifluoromethyl-benzenesulfonamide, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.
59. The compound according to claim 53, selected from the group consisting of trans-4-bromo-N-[4-(2-diisopropylamino-ethoxy)-cyclohexyl]-N-methyl-benzenesulfonamide, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.
60. The compound according to claim 45, wherein V is S.
61. The compound according to claim 60, wherein W is COO.
62. The compound according to claim 60, wherein W is SO₂.

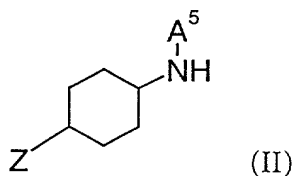
63. The compound according to claim 45, wherein V is-CH₂-.
64. The compound according to claim 63, wherein W is COO.
65. The compound according to claim 64, wherein A¹¹ is H.
66. The compound according to claim 65, selected from the group consisting of trans-methyl-[4-(5-methylamino-pentyl)-cyclohexyl]-carbamic acid 4-trifluoromethyl-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.
67. The compound according to claim 64, wherein A¹¹ is methyl.
68. The compound according to claim 67, selected from the group consisting of trans-{4-[5-(allyl-methyl-amino)-pentyl]-cyclohexyl}-methyl-carbamic acid 4-trifluoromethyl-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.
69. The compound according to claim 67, selected from the group consisting of trans-{4-[5-(allyl-methyl-amino)-pentyl]-cyclohexyl}-methyl-carbamic acid 4-bromo-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.
70. The compound according to claim 67, selected from the group consisting of trans-{4-[5-(allyl-methyl-amino)-pentyl]-cyclohexyl}-methyl-carbamic acid 4-chloro-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.
71. The compound according to claim 67, selected from the group consisting of trans-{4-[4-(allyl-methyl-amino)-butyl]-cyclohexyl}-methyl-carbamic acid 4-chloro-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

72. The compound according to claim 64, wherein A¹¹ is ethyl.
73. The compound according to claim 72, selected from the group consisting of trans-(4-{5-[ethyl-(2-hydroxy-ethyl)-amino]-pentyl}-cyclohexyl)-methyl-carbamic acid 4-trifluoromethyl-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.
74. The compound according to claim 72, selected from the group consisting of trans-(4-{5-[ethyl-(2-hydroxy-ethyl)-amino]-pentyl}-cyclohexyl)-methyl-carbamic acid 4-bromo-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.
75. The compound according to claim 72, selected from the group consisting of trans-(4-{3-[ethyl-(2-hydroxy-ethyl)-amino]-propyl}-cyclohexyl)-methyl-carbamic acid 4-chloro-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.
76. The compound according to claim 63, wherein W is SO₂.
77. The compound according to claim 76, selected from the group consisting of trans-N-{4-[5-(allyl-methyl-amino)-pentyl]-cyclohexyl}-N-methyl-4-trifluoromethyl-benzenesulfonamide, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.
78. The compound according to claim 76, selected from the group consisting of trans-N-(4-{5-[ethyl-(2-hydroxy-ethyl)-amino]-pentyl}-cyclohexyl)-N-methyl-4-trifluoromethyl-benzenesulfonamide, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.
79. The compound according to claim 45, wherein V is -C=C-.
80. The compound according to claim 79, wherein W is COO.
81. The compound according to claim 79, wherein W is SO₂.

82. The compound according to claim 81, selected from the group consisting of trans-(1E)-N-methyl-N-{4-[3-(methyl-propyl-amino)-propenyl]-cyclohexyl}-4-trifluoromethyl-benzenesulfonamide, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.
83. The compound according to claim 81, selected from the group consisting of trans-(1E)-N-(4-{3-[ethyl-(2-hydroxy-ethyl)-amino]-propenyl}-cyclohexyl)-N-methyl-4-trifluoromethyl-benzenesulfonamide, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.
84. The compound according to claim 45, wherein V is $-C\equiv C-$.
85. The compound according to claim 84, wherein W is COO.
86. The compound according to claim 85, selected from the group consisting of trans-{4-[3-(allyl-methyl-amino)-prop-1-ynyl]-cyclohexyl}-methyl-carbamic acid 4-chloro-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.
87. The compound according to claim 85, selected from the group consisting of trans-(4-{5-[ethyl-(2-hydroxy-ethyl)-amino]-pent-1-ynyl}-cyclohexyl)-methyl-carbamic acid 4-chloro-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.
88. The compound according to claim 85, selected from the group consisting of trans-methyl-{4-[3-(methyl-propyl-amino)-prop-1-ynyl]-cyclohexyl}-carbamic acid 4-chloro-phenyl ester, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.
89. The compound according to claim 84, wherein W is SO₂.
90. The compound according to claim 89, selected from the group consisting of trans-N-[4-(4-dimethylamino-but-1-ynyl)-cyclohexyl]-N-methyl-4-trifluoromethyl-

benzenesulfonamide, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.

91. The compound according to claim 89, selected from the group consisting of trans-N-methyl-N-{4-[4-(methyl-propyl-amino)-but-1-ynyl]-cyclohexyl}-4-trifluoromethyl-benzenesulfonamide, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.
92. The compound according to claim 89, selected from the group consisting of trans-N-(4-{4-[ethyl-(2-hydroxy-ethyl)-amino]-but-1-ynyl}-cyclohexyl)-N-methyl-4-trifluoromethyl-benzenesulfonamide, pharmaceutically acceptable salts thereof and pharmaceutically acceptable esters thereof.
93. A process for the manufacture of a compound according to claim 1, comprising reacting a compound of formula (II)



wherein

A^5 is as defined in claim 1,

Z is a group $(A^1, A^2)_N-C(A^3, A^4)-(CH_2)_m-V-(CH_2)_n$ or $HO-(CH_2)_n$, wherein A^1, A^2, A^3, A^4, V, m and n are defined as in claim 1,

with $ClSO_2-A^6, ClCOO-A^6, ClCSO-A^6, OCN-A^6, SCN-A^6, HOOC-A^6$, or $ClSO_2NR^1-A^6$, wherein A^6 is as defined in claim 1.

94. A pharmaceutical composition comprising a compound according to claim 1 and at least one of a pharmaceutically acceptable carrier or a pharmaceutically acceptable adjuvant.
